ABSTRACTS – POSTER

937 Myocardial Infarction: Basic I

Tuesday, March 26, 1996, 9:00 a.m.–11:00 a.m.
Orange County Convention Center, Hall E
Presentation Hour: 10:00 a.m.–11:00 a.m.

937-29 Proportionate Decreases in Myocardial O_2 Consumption and Segmental Function Following Mild Reversible Ischemia — Responses of Hibernation/Preconditioning Persist for Hours and Occur Globally as Well as Regionally

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Acute studies in open-chest animals and isolated hearts indicate that myocardial metabolic demand can be downregulated during periods of mild-to-moderate flow reduction. In order to determine whether this beneficial adaptive response can be sustained following mild reversible ischemia, left circumflex (LC) and anterior descending (LAD) flow, segmental shortening (SS) and coronary sinus O_2 levels have been measured in eight chronically instrumented dogs following sustained 10–40% reductions in LC flow or repeated 2-minute LC occlusions. LC SS and O_2 consumption decreased consistently following both interventions, averaging 79 ± 2.9 [SEM] and 82 ± 3.6% of control values two hours after the interventions ($p < 0.01$, paired t, in both cases). Reductions in O_2 consumption involved decreases in both LC flow (12 ± 2.3%) and A-V O_2 extraction (7.9 ± 2.0%). LAD flow and segmental function also decreased following LC flow restriction, but by smaller amounts (6.8 ± 1.8% and 10 ± 1.6%). All parameters returned to pre-intervention values within 24 hours. We conclude: (1) Proportionate reductions in myocardial metabolism and function develop rapidly and persist for hours following mild reversible ischemia; (2) The reductions are consistent with both "short-term" hibernation and preconditioning; (3) The reductions occur globally as well as regionally and, in this preparation, can be separated from the myocardial stunning which follows more severe ischemia.

937-30 Attenuated Purine Release From Preconditioned Rabbit Myocardium Is Unrelated to Protection

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Less purine is released from the myocardium during a second 5-min coronary occlusion than during a first occlusion. Because the heart is also in a preconditioned (PC) state during the second ischemia, this study tested whether that reduced purine release is related to the same mechanism responsible for the protection. Coronary effluent from isolated rabbit hearts was collected and purine (adenosine + inosine + hypoxanthine) levels were measured. Hearts underwent 2 cycles of 5-min global ischemia separated by 10 min of reperfusion. Untreated hearts released 155 ± 14 nmol purines/g wet weight after the first ischemia but only 104 ± 16 nmol/g following the second ischemia ($p < 0.05$). When 8-(p-sulfophenyl) theophylline (100 μM), which prevents the anti-infarct effect of PC by blocking adenosine receptors, was in the perfusate, the purine release pattern was not altered (151 ± 13 nmol/g after the first dropping to 120 ± 8 nmol/g after the second ischemia). Thus attenuated purine release continued despite blockade of protection. 5-min exposure of the heart to either adenosine (10 μM) or phenylephrine (0.1 μM) mimics ischemia and puts the heart into a PC state. Yet despite the pretreatment which successfully PCed the heart, purine release during an initial occlusion was not reduced (144 ± 16 nmol/g and 148 ± 15 nmol/g for adenosine and phenylephrine, resp.). However, purine release did fall during a second ischemia (84 ± 12 nmol/g and 111 ± 9 nmol/g, resp.). Thus, the release of purines following the second ischemic period was always attenuated regardless of whether or not the heart was in a protected state, and hence must be unrelated to the mechanism of PC's protection.

937-31 Cardioprotective Effect of Monophosphoryl Lipid A Is Mediated by Opening K_{ATP} Channels in Rabbit Heart

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Monophosphoryl lipid A (MLA), a nonpyrogenic derivative of endotoxin, has been shown to protect the heart from ischemia/reperfusion induced infarction and stunning, although its mechanisms of action still remain unknown. Literature has shown that the K_{ATP} channel blocker, glibenclamide, can attenuate endotoxin induced effects such as tissue factor and TNF-α release from macrophages and lethality in galactosamine loaded mice. We hypothesized that MLA pretreatment may elicit cardiac protection by opening or priming K_{ATP} channel, a known effector of ischemic preconditioning. Rabbits were randomly assigned to one of the four groups. (1) vehicle control [n = 9]; (2) MLA pretreated [n = 7]; (3) glibenclamide control [n = 8]; and (4) MLA + glibenclamide [n = 7]. MLA (35 μg/kg I.V.) or vehicle was given 24 hours before ischemia. Glibenclamide (0.3 mg/kg) was intravenously injected 30 minutes prior to ischemia. All rabbits underwent 30 minutes of coronary artery occlusion followed by 3 hours of reperfusion. Hemodynamics, blood gases and glucose, were monitored throughout the experiment. Risk area (expressed as AR/LV%) was delineated by Unisperse® dye, and infarct size (expressed as AN/AR%) was measured by tetrazolium staining.

Groups	Control	MLA	Control + Glib	MLA + Glib
AR/LV %	51.3 ± 2.9%	45.3 ± 5.5%	51.6 ± 2.6%	55.7 ± 3.0%
AN/AR %	21.0 ± 3.6%	7.5 ± 3.0%*	16.6 ± 2.7%	16.2 ± 1.71%

Average ± SEM. *$p < 0.01$

MLA pretreatment reduced infarct size by 64.3% compared to control (*$p < 0.01$). Glibenclamide alone did not alter infarct size from that of vehicle control rabbits. However, MLA pretreatment lost its protection in the event of peri-ischemic glibenclamide treatment (p = NS vs. control). These data indicate that MLA may pharmacologically mimic preconditioning through activating myocardial K_{ATP} channels.

937-32 Right Ventricular Infarction Causes Sympathetic Denervation in Viable Myocardium at the RVOT Side of the Peri-Infarct Area

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Efferent sympathetic pathways to the right ventricle (RV) differ from those to the left ventricle (LV). While the autonomic effects of LV infarction have been studied, those of RV infarction have not and was the purpose of this study. We measured the ventricular effective refractory period (ERP) shortening in response to bilateral ansae subclaviae stimulation (SS, 2–4 Hz, 3 V, 4 ms) and during IV infusion of norepinephrine (NE, 0.25 mcg/kg/min) at two outflow tract (RVOT), two septal and four lateral sites on the RV free wall before and after coronary ligation (group 1, n = 8 dogs) or latex injection (group 2, n = 9 dogs), into a marginal branch of the right coronary artery. SS before coronary occlusion significantly shortened the ERP (ΔERP = 15 ± 6 ms) at all (n = 136) sites and became attenuated at 12 RVOT sites and abolished at 16 RVOT sites (ΔERP = 6.4 ± 4.2 ms and 0.2 ± 2.1 ms respectively, $P < 0.01$) and did not change significantly at the lateral and septal sites (ΔERP = 11.7 ± 4.2 ms) 180 min after coronary occlusion. NE infusion 200 min after coronary occlusion shortened ERP at all lateral and septal (n = 102, ΔERP = 12.3 ± 3.8 ms) sites and 31 of the 34 RVOT sites (ΔERP = 11.5 ± 3.2 ms), indicating normal responsiveness. The ERP of the remaining 3 RVOT sites did not respond significantly to NE infusion (ΔERP = 1.2 + 2 ms). Conclusion: RV infarction causes sympathetic denervation at viable sites at the RVOT side of the infarct area and might contribute to the development of ventricular tachyarrhythmias during both the acute and chronic stages of myocardial infarction involving the RV.

TUESDAY POSTER